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| 10/524,193 | 02/11/2005 | Nobutaka Nakashima | 081356-0232 | 4133 |
| 22428 7590 01/30/2009 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007 | | | EXAMINER POPA, ILEANA | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/524,193

Applicant(s)

NAKASHIMA ET AL.

Examiner

ILEANA POPA

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2008.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29 and 31 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 29 and 31 is/are rejected.
7) ☒ Claim(s) 29 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-8508)
Paper No(s)/Mail Date 10/16/2008
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/16/2008 has been entered.

Claims 1-28, 30, and 32-42 have been cancelled. Claims 29 and 31 have been amended.

Claims 29 and 31 are pending and under examination.

2. The rejection of claims 29 and 31 under 35 U.S.C. 103(a) as being unpatentable over De Mot et al. (Microbiology, 1997, 143: 3137-3147), in view of each Takano et al. (Gene, 1995, 166: 133-137), Whyte et al. (Appl Environ Microbiol, 1998, 64: 2578-2584), and Chiu et al. (J Biol Chem, 1999, 274: 20578-20586) is withdrawn in response to Applicant's amendments to the claims filed on 09/17/2008.

New Rejections/Objections

Claim Objections

3. Claim 29 is objected to because of the following informalities: the claim recites "a *TipA*-LG10 promoter" and "a *TipA* gene". Since there is only one *TipA*-LG10 promoter

and one *TipA* gene, appropriate correction to "the *TipA*-LG10 promoter" and "the *TipA* gene" is required. Similarly, the claim recites the vector pTip-LNH1 "having a nucleotide sequence represented by SEQ ID NO: 110". Since pTip-LNH1 has a specific sequence, correction to ""having the nucleotide sequence set forth by SEQ ID NO: 110" is suggested.

4. Claim 29 is objected to because of the recitation of "*TipA*-LG10". Abbreviations, unless otherwise obvious and /or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 29 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 29 recites an expression vector comprising different elements however the claim is silent with respect to the arrangement of these elements within the vector. Since it is not clear how these elements relate to each other, the metes and bounds of the claim cannot be determined and the claim is indefinite. Amending the claim to recite the 5' to 3' order of the different elements within the vector would obviate this rejection.

Claims 31 is rejected for being dependent from the rejected claim 29 and also for failing to further clarify the basis of the rejection.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 29 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Mot et al. (Microbiology, 1997, 143: 3137-3147, Applicant's IDS), in view of each Takano et al. (Gene, 1995, 166: 133-137, Applicant's IDS), Olins et al. (Gene, 1988, 73: 227-235, of record), and Chiu et al. (J Biol Chem, 1999, 274: 20578-20586, of record).

De Mot et al. teach isolation of a cryptic plasmid from *R. erythropolis* and the use of this plasmid to construct a shuttle *E. coli-Rhodococcus* expression vector (i.e., a vector comprising a DNA sequence essential to autonomous replication in *Rhodococcus* and a DNA sequence essential to replication in *E. coli*), wherein the vector can be used with a wide range of *Rhodococcus* species, including *R. erythropolis* (claims 29 and 31) (Abstract, p. 3137, columns 1 and 2, p. 3138, column 1). De Mot et al. do not teach their vector as comprising a thiostrepton resistance gene or the *tipA*-LG10 promoter (claim 29). However including such in their vector is suggested by the

prior art. For example, Takano et al. teach *tipA* promoter/thiostrepton inducible system to construct inducible expression vectors for expression of proteins in *Streptomyces* spp, wherein the inducible expression vectors also contain the thiostrepton resistance gene (Abstract, p. 133, column 2, p. 134, column 1). Takano et al. also teach that such vectors can be used for induced expression of proteins that inhibit host cell growth when the cells are grown at the suitable temperature (p. 133, column 2). Takano et al. do not teach *tipA*-LG10 promoter. Olins et al. teach that the use ribosome-binding site derived from the region located upstream from gene 10 of the phage T7 (g10-L) in expression vectors dramatically increases the expression of a wide variety of foreign genes (Abstract, p. 228, column 1 bridging column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the expression vector of De Mot et al. by introducing the *tipA* promoter/thiostrepton inducible system of Takano et al. together with the thiostrepton resistance gene, with a reasonable expectation of success. Additionally, it would have been obvious to one of skill in the art, at the time the invention was made, to further modify the vector of De Mot et al. and Takano et al. by replacing the RBS of the *tipA* promoter with the g10-L of Olins et al. to obtain the *tipA*-LG10 promoter, with a reasonable expectation of success (it is noted that the specification defines *tipA*-LG10 promoter as the *tipA* promoter and the RBS derived from lambda phage gene 10; see paragraph 0152). The motivation to use the *tipA* promoter/thiostrepton inducible system is provided by Takano et al., who teach that (i) inducible system should be used for expression of proteins that inhibit host cell growth, and (ii) *tipA* promoter/thiostrepton is a widely used and very efficient inducible system

(p. 133, column 2). The motivation to use the thiostrepton resistance gene is also provided by Takano et al., who teach the need to provide resistance to thiostrepton upon induction (p. 134, column 1, first full paragraph). The motivation to further include g10-L (i.e., to obtain the *tipA*-LG10 promoter) is provided by Olins et al., who teach dramatic enhancement of protein expression by g10-L. One of skill in the art would have been expected to have a reasonable expectation of success in making and using such an expression vector because the art teaches that such expression vectors can be successfully made and used. With respect to the limitation of the vector comprising a multicloning site and a transcription terminator, such are inherent to any expression vectors; all expression vectors have a multicloning site and transcription terminators. With respect to the limitation of an inducer cassette comprising a promoter driving the expression of the *tipA* gene, the vector of De Mot et al. and Takano et al. must necessarily contain this because, in the absence of *tipA* gene product, the thiostrepton/*tipA* promoter inducible system does not work (see Chiu et al., p. 20580, column 2, first full paragraph). With respect to the specific vector pTIP-LNH1 set forth by SEQ ID NO: 110 recited in the instant claim 29, it is noted that there is no evidence on the record that the vector backbone results in a construct exhibiting an unexpected property. The essential components (i.e., the expression cassette comprising the *tipA*-LG10 promoter, a multicloning site for the insertion of a foreign gene and a transcription termination sequence, the inducer cassette, the DNA region essential for the autonomous replication in *R. erythropolis*, and the thiostrepton resistance gene) and a vector comprising all these essential elements are taught by the combined art above. The

difference between the claimed vector and the vector taught by the cited art is the vector backbone. The backbone is not significant if it does not provide a novel feature. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

9. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Ileana Popa/
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